

Application No.: 09/167 289

Applicant: Harry C. Diaz

Filed: Sept. 29, 1998

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REMARKS

The following remarks are in response to the Office Action mailed July 30, 2002. Claims 1 and 2 have been amended to clarify the location of the antisense molecule in relation to the stem loop structures. No new matter has been added. Upon entry of the amendment, claims 1-13 and 15 will be pending. Applicant respectfully requests reconsideration of the pending claims.

A. Rejection Under 35 U.S.C. § 112, First Paragraph (Written Description)

The rejection of claims 1-13 and 15 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, has possession of the claimed invention, is respectfully traversed.

Applicant disagrees with the Examiner's assertion that the specification allegedly does not teach that Applicant was in possession of a representative number of species of the claimed constructs at the time the invention was made. Applicant submits that the specification provides ample support for the nucleic acid constructs and methods claimed. Indeed, as acknowledged by the Examiner, Applicant is in possession (i.e., Applicant has provided adequate written description) of antisense constructs flanked by 5' and 3' U1 snRNA stem loop structures. Applicant respectfully disagrees with the Examiner's assertion that the specification allegedly does teach a representative number of species to support the breadth of nucleic acid constructs and methods presently claimed. For example, claim 1 is drawn to a well defined nucleic acid construct for suppressing gene expression comprising in a 5' to 3' orientation a stem loop structure, an antisense nucleic acid, and a 3' stem loop structure, wherein the antisense nucleic acid is flanked by the stem loop structures and with the proviso that the antisense nucleic acid is not within the stem loop structures. The specification fully describes and defines each component of the

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construct (see, e.g., specification page 7, lines 12-23; page 8, lines 18-25). Accordingly, contrary to the Examiner's assertion, the present claims are not drawn to any and all nucleic acid constructs. Instead, the claims are drawn to the well-defined set of constructs disclosed in the specification having particular elements in a specific orientation.

With specific reference to the stem loop structures, Applicant respectfully disagrees with the Examiner's assertion that those skilled in the art allegedly would not know what other possible stem loops would be functional equivalents to the U1 snRNA stem loops. Applicant submits that the U1 snRNA stem loops are set forth for exemplary purposes only. The requirements for functionally equivalent stem loops are clearly and coherently disclosed in the specification (see, e.g., specification page 7, lines 12 to page 8, line 6), which also describes a U3 stem loop structure as an alternative. Based on this disclosure, it is submitted that those skilled in the art could readily determine functional equivalents to the U1 snRNA stem loops.

With specific reference to the antisense nucleic acid, Applicant respectfully disagrees with the Examiner's assertion that the written description requirement allegedly has not been satisfied by the teachings of the present specification. Those skilled in the art recognize that the antisense nucleic acid can be directed toward any target nucleic acid. Therefore, any antisense nucleic acid which includes sequences capable of activity, i.e., hybridizing with its complementary target and affecting expression of that target can be used in invention constructs. For example, antisense sequences can be directed to the 5' or 3' termini of the target message, to splice junctions, or to internal sequences. Clearly, those skilled in the art would readily be able to determine which sequences are appropriate antisense nucleic acids to utilize in an invention construct.

Thus, when the claims are construed in view of the specification, those skilled in the art would readily recognize that the specification provides sufficient information to

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demonstrate possession of the presently claimed constructs. Accordingly, reconsideration and withdrawal of the rejection of claims 1-13 and 15 under 35 U.S.C. § 112, first paragraph are respectfully requested.

B. Rejections Under 35 U.S.C. § 102(a)

The rejection of claims 1 to 12 under 35 U.S.C. § 102(a) as allegedly being anticipated by Michienzi *et al.* (Proc. Natl. Acad. Sci. USA, 993:7219 (1996)) is respectfully traversed.

Applicant's invention distinguishes over Michienzi by reciting a nucleic acid construct for suppressing gene expression comprising in 5' to 3' orientation, a 5' stem loop structure, an antisense nucleic acid, and a 3' stem loop structure, wherein the stem loop structures flank the antisense nucleic acid and and with the proviso that the antisense nucleic acid is not within the 5' or 3' stem loop structures. While not wishing to be bound by a particular theory, it is believed that since the natural hairpins in U snRNAs protect the molecules from rapid turnover (presumably by blocking the access of exonucleases), modified snRNAs might serve as excellent vehicles for regulatory sequences such as antisense, ribozymes, etc. Implicit in this approach is the need to place the regulatory sequence between unaltered 5' and 3' hairpins - not 5' to both hairpins or within either hairpin, as set forth in the prior art.

Contrary to the present invention, Michienzi describes nucleic acid constructs in which the stem loop III of U1 snRNA is modified by the addition of a hammerhead ribozyme within the stem loop structure. Applicant's constructs contain unmodified stem loop structures which flank an antisense nucleic acid sequence, wherein the antisense nucleic acid sequence is an active sequence. The antisense sequence of Applicant's constructs are not contained within either of the stem loop structures.

Moreover, Applicants respectfully disagree with the Examiner's assertion that Michienzi's construct contains "unmodified" stem loops. The allegedly unmodified U1-Rz

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construct referred to by the Examiner on page 7219, column b, lines 39-42, is shown graphically in Figure 1 of Michienzi. Michienzi's allegedly unmodified U1-Rz construct is a U1 snRNA that has a hammerhead ribozyme nucleic acid sequence inserted into the stem-loop III nucleic acid sequence. Michienzi's modified construct (U1-Rz_m) is a construct in which the nucleic acid sequence forming the catalytic core of the hammerhead, *i.e.*, CUGAUGA, has C replaced by G (see page 7220, column b, lines 26-32). Such modification renders the catalytic activity of the ribozyme inactive. In contrast, the antisense molecules as claimed in Applicant's invention are active molecules. Accordingly, reconsideration and withdrawal of the rejection of claims 1 to 12 under 35 U.S.C. § 102(a) are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all of the pending claims is respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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Exhibit A
Marked up Version of Claims to Show Changes

Please amend the claims as follows:

1. (Three times amended) A nucleic acid construct for suppressing gene expression comprising in 5' to 3' orientation:
[an unmodified] a 5' stem loop structure;
an antisense nucleic acid; and
[an unmodified] a 3' stem loop structure, wherein the antisense nucleic acid is capable of having activity and is flanked by the stem loop structures and with the proviso that the antisense nucleic acid is not within the 5' or 3' stem loop structures.
2. (Twice Amended) The nucleic acid construct of claim 1, wherein the [unmodified] stem loop structures are [unmodified] U snRNA structures.